Stem Cell Rev and Rep (2015) 11:280–287
DOI 10.1007/s12015-014-9583-3

Mesenchymal Stem Cells: A Friend or Foe in Immune-Mediated Diseases

Marina Gazdic · Vladislav Volarevic · Nebojsa Arsenijevic · Miodrag Stojkovic

Published online: 16 January 2015

Abstract Mesenchymal stem cells (MSCs) are adult, self-renewable, multipotent cells that can be found in almost all postnatal tissues. Because of their capacity for self-renewal and differentiation into tissues of mesodermal origin and due to their immunomodulatory ability, MSCs are used in many preclinical and clinical studies as possible new therapeutic agents for the autoimmune or degenerative diseases treatment. In dependence of inflammatory environment to which they are exposed to, MSCs adopt immunosuppressive or pro-inflammatory phenotype. In the presence of high levels of pro-inflammatory cytokines or through activation of Toll-like receptor (TLR)-3, MSCs adopt an immune-suppressive phenotype and suppress the proliferation, activation and effector function of professional antigen presenting cells (dendritic cells, macrophages, B lymphocytes), T lymphocytes, NK cells, NKT cells, and neutrophils. During the early phase of inflammation, through TLR4 activation and in the presence of low levels of inflammatory cytokines, MSCs adopt a pro-inflammatory phenotype, promote neutrophil and T cell activation and enhance immune response. Here we review the current findings on the immunoregulatory plasticity of MSCs involved in regulation of immune response.

Keywords Mesenchymal stem cells · Inflammation · Therapy · Immunosuppression · Autoimmunity

M. Gazdic · V. Volarevic (✉) · N. Arsenijevic · M. Stojkovic
Center for Molecular Medicine and Stem Cell Research, Faculty of Medical Sciences, University of Kragujevac, 69 Svetozara Markovica Street, 34000 Kragujevac, Serbia
e-mail: drvladislavv@gmail.com

M. Stojkovic
Spebo Medical, Leskovac, Serbia

Introduction

Mesenchymal stem cells (MSCs), also known as mesenchymal stromal cells, are adult, self-renewable, fibroblast-like, multipotent cells characterized by the ability to differentiate into the tissues of mesodermal origin [1, 2]. Recent data suggest that plasticity, one of major characteristics of MSC, should be extended to nonmesenchymal lineages of neuroectodermal (neurons, astrocytes, and oligodendrocytes) or endodermal (hepatocytes) origin [3].

MSCs are most frequently isolated from bone marrow, adipose tissue, umbilical cord blood, but can be found in almost all postnatal tissues [4]. The origin of MSCs and their developmental derivation is still not completely resolved issue. Battula and co-workers demonstrated that epithelial-mesenchymal transition-derived cells are similar to MSCs in gene expression, multilineage differentiation, and ability to migrate towards wound sites [5]. Takashima and co-workers showed that the first MSC progenitors in the embryo are derived from Sox1+ neuroepithelial cells [6]. However, they demonstrated that, during embryogenesis, Sox1+ neuroepithelial cells supply only the earliest wave of MSC differentiation, but is later replaced by MSCs from other origins in postnatal development [6]. This observation does not rule out a possibility that paraxial mesoderm has potential to give rise to MSCs under other appropriate conditions. Most findings support the hypothesis that MSCs originate from the perivascular cells [7]. Blood vessel walls of many organs harbor a reserve of progenitor cells that may be integral to the origin of the elusive MSCs. Long-term cultured perivascular cells, principally pericytes, isolated from multiple human organs expressed MSC markers and exhibited osteogenic, chondrogenic, and adipogenic potentials [7].

In order to create a broader consensus for more uniform characterization of MSCs, and facilitate the exchange of data among investigators, the International Society for Cellular